

IN THE CLAIMS:

Please **cancel** claim 16.

Please **amend** claims 1, 12, 21, 25, and 29 as follows:

1. (Amended) A method of determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize a thioamide or a thiocarbonyl, said method comprising detecting a mutation in an EtaA gene (SEQ ID NO:1) in said bacterium, which mutated gene encodes an amino acid sequence which differs from that of SEQ ID NO:2, wherein detection of the mutation is indicative of decreased ability to oxidize a thioamide or a thiocarbonyl.

12. (Amended) A method of claim 11, wherein said mutation in said EtaA gene is selected from the group consisting of (a) a frameshift mutation consisting of a deletion at position 65, an addition at position 567, and an addition at position 811, and (b) a single nucleotide polymorphism which causes an amino acid substitution selected from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P.

21. (Amended) A method of screening an individual for a *Mycobacterium tuberculosis* bacterium resistant to treatment by a thioamide or a thiocarbonyl drug, comprising

(a) obtaining a biological sample containing said bacterium from said individual, and

(b) detecting a mutation in an EtaA gene (SEQ ID NO:1) in said bacterium, which mutated gene encodes an amino acid sequence which differs from that of SEQ ID NO:2, wherein detection of the mutation is indicative said bacterium is resistant to treatment by a thioamide or a thiocarbonyl drug.

25. (Amended) A kit for determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize a thioamide or a thiocarbonyl, the kit comprising:

- (a) a container, and
- (b) primers for specifically amplifying an EtaA gene of said bacterium or a portion of said EtaA gene containing a mutation affecting the ability of the bacterium to oxidize a thioamide.

29. (Amended) A kit of claim 28, wherein said mutation in said EtaA gene is selected from the group consisting of (a) a frameshift mutation consisting of a deletion at position 65, an addition at position 567, and an addition at position 811, and (b) a single nucleotide polymorphism which causes an amino acid substitution selected from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P

Please **add** the following new claims:

34. (New) A method of determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize a thioamide or a thiocarbonyl selected from the group consisting of ethionamide, thiacetazone and thiocarlide, said method comprising detecting a mutation in an EtaA gene (SEQ ID NO:1) in said bacterium, which mutated gene encodes an amino acid sequence which differs from that of SEQ ID NO:2, wherein detection of the mutation is indicative of decreased ability to oxidize ethionamide, thiacetazone or thiocarlide.

35. (New) The method of claim 34, wherein the mutation is a frameshift mutation selected from the group consisting of: a deletion at position 65, an addition at position 567, and an addition at position 811.

36. (New) The method of claim 34, wherein the mutation is a single nucleotide polymorphism which causes an amino acid substitution in an amino acid

sequence encoded by said EtaA gene compared to an amino acid sequence of SEQ ID NO:2.

37. (New) The method of claim 36, wherein the single nucleotide polymorphism causes an amino acid substitution selected from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P.

38. (New) A method of claim 34 wherein the mutation is detected by

- (a) amplifying the EtaA gene, or a portion thereof containing the mutation, with a set of primers to provide an amplified product,
- (b) sequencing the amplified product to obtain a sequence, and
- (c) comparing the sequence of the amplified product with the sequence of a wild-type EtaA gene (SEQ ID NO:1) or portion thereof,

wherein a difference between the sequence of the amplified product and the sequence of the wild-type EtaA gene or portion thereof indicates the presence of a mutation.

39. (New) A method of claim 38, wherein said amplification is by polymerase chain reaction.

40. (New) A method of claim 34, wherein said mutation is detected by hybridizing DNA from said bacterium to a test nucleic acid under stringent conditions.

41. (New) A method of claim 40, wherein either said DNA from said bacterium or said test nucleic acid is immobilized on a solid support.

42. (New) A method of claim 34, wherein said mutation is detected by

- (a) subjecting said EtaA gene to digestion by restriction enzymes,
- (b) separating the resulting restriction products to form a pattern of restriction fragment lengths, and

(c) comparing the pattern of restriction fragment lengths to a pattern of restriction fragment lengths formed by subjecting a known EtaA gene to the same restriction enzymes.

43. (New) A method of claim 42, wherein said known EtaA gene is selected from the group consisting of (a) a frameshift mutation consisting of a deletion at position 65, an addition at position 567, and an addition at position 811, and (b) a single nucleotide polymorphism which causes an amino acid substitution selected from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P.

44. (New) A method of screening an individual for a *Mycobacterium tuberculosis* bacterium resistant to treatment by a thioamide or a thiocarbonyl drug, selected from the group consisting of ethionamide, thiacetazone and thiocarlide, comprising

(a) obtaining a biological sample containing said bacterium from said individual, and

(b) detecting a mutation in an EtaA gene (SEQ ID NO:1) in said bacterium, wherein detection of the mutation is indicative said bacterium is resistant to treatment by ethionamide, thiacetazone or thiocarlide.

45. (New) A method of claim 44, wherein the mutation is detected by  
(a) amplifying the EtaA gene with a set of primers to provide an amplified product,

(b) sequencing the amplified product to obtain a sequence, and

(c) comparing the sequence of the amplified product with the sequence of a wild-type EtaA gene (SEQ ID NO:1),

wherein a difference between the sequence of the amplified product and the sequence of the wild-type EtaA gene indicates the presence of a mutation.

46. (New) A kit for determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize a thioamide or a thiocarbonyl selected from the group consisting of ethionamide, thiacetazone and thiocarlide, the kit comprising:

- (a) a container, and
- (b) primers for amplifying an EtaA gene of said bacterium or a portion of said EtaA gene containing a mutation affecting the ability of the bacterium to oxidize. ethionamide, thiacetazone or thiocarlide

47. (New) A kit of claim 46, further comprising a mutated EtaA gene for use as a positive control.

48. (New) A kit of claim 47, wherein said mutated EtaA gene is selected from the group consisting of (a) a frameshift mutation consisting of a deletion at position 65, an addition at position 567, and an addition at position 811, and (b) a single nucleotide polymorphism which causes an amino acid substitution selected from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P.

## REMARKS

### **I. Status of the Claims**

Claims 1-5, 8-12, 21, 22, 25, 28, 29 and 34-48 are pending. Claims 6, 7, 23, 24, 26, and 27 have been previously cancelled, claims 13-15, 17-20, and 30-33 have been withdrawn as drawn to non-elected inventions, claim 16 is cancelled herein, and claims 34-48 have been added herein.

### **II. The Present Amendment**

No new matter has been added by the present amendments.

The amendments to paragraphs 30 and 62 of the specification reword the recitation of two websites so that they will not form active hyperlinks when the